

Indicator: Blood Cotinine Level (102, 107)

Environmental tobacco smoke (ETS) contains a mixture of toxic chemicals, including known human carcinogens. Persistent exposure to ETS is associated with an increased risk for lung cancer and other diseases (CDC, 2003). Children are at particular risk from exposures to ETS, which may exacerbate existing asthma among susceptible children and also greatly increase the risk for lower respiratory-tract illness, such as bronchitis and pneumonia, among younger children (CDC, 2003).

Exposure to ETS leaves traces of specific chemicals in people's blood, urine, saliva, and hair. In its nationwide health surveys, the Centers for Disease Control and Prevention (CDC) measures blood concentrations of cotinine to assess exposure to ETS. Cotinine is a chemical that forms inside the body following exposure to nicotine, an ingredient in all tobacco products and a component of ETS. Following nicotine exposures, cotinine can usually be detected in blood for at least 1 or 2 days (Pirkle et al., 1996). Active smokers almost always have blood cotinine levels higher than 10 nanograms per milliliter (ng/mL), while non-smokers exposed to low levels of ETS typically have blood concentrations less than 1 ng/mL (CDC, 2003). Following heavy exposure to ETS, non-smokers can have blood cotinine levels between 1 and 15 ng/mL. As part of the National Health and Nutrition Examination Survey III (NHANES III, 1988-1991), CDC determined that the median blood serum level (50th percentile) of cotinine among non-smokers in the general U.S. population was 0.20 ng/mL (Pirkle et al., 1996).

This indicator reflects blood cotinine concentrations in ng/mL for the United States population, aged three year and older, as measured in the 1999-2000 National Health and Nutrition Examination Survey (NHANES). NHANES is a series of surveys conducted by CDC's National Center for Health Statistics (NCHS) that is designed to collect data on the health and nutritional status of the civilian, non-institutionalized U.S. population using a complex, stratified, multistage, probability-cluster design. Beginning in 1999, NHANES became a continuous and annual national survey. These data are presented here as a baseline with the intent of reporting trends in the future.

What the Data Show

In NHANES 1999-2000 (see Table 102_107Cotinine), the median serum levels among non-smokers nationwide was 0.06 ng/mL. This marks a 70% decrease from levels measured in the 1988-1991 NHANES III survey — a reduction that suggests a marked decrease in exposure to ETS (Pirkle et al., 1996). Further, decreased blood cotinine levels were observed in each of the population groups defined by age, sex, and race/ethnicity (CDC, 2003).

Table 102-107Cotinine shows the results of the NHANES 1999–2000 survey, both for the overall population and for different sub-populations. These data reveal three current trends: (1) non-smoking males have higher cotinine levels than non-smoking females; (2) of the ethnic groups considered, non-Hispanic African Americans had the highest cotinine levels; and (3) on average, people below age 20 have higher levels of blood cotinine than people aged 20 years and older.

Indicator Limitations

- NHANES selects a representative sample of the civilian, non-institutionalized population in the United States using a complex, stratified, multistage, probability-cluster design. Beginning in 1999, NHANES became a continuous and annual national survey. With only 2 years of data in NHANES 1999-2000, instead of the 6-years for NHANES III (1988-1994), some differences exist that may limit the underlying data with respect to completeness or representative of coverage.

- The sample size is smaller and the number of geographic units in the sample is more limited. The current 1999-2000 NHANES survey is nationally representative but it is subject to the limits of increased sampling error due to (1) the smaller number of individuals sampled in the annual sample and (2) the smaller number of Primary Sampling Units (PSUs) [see description below] available for each annual sample. Therefore, the sample size for any 1-year period is relatively small, possibly resulting in large variability for U.S. population estimates, especially those for narrowly defined demographic groups or other specific subgroup analyses.
- For NHANES 1999-2000, the first stage of selection was the PSU-level. The PSUs were defined as single counties. For a few PSUs, the county population was too small and those counties were combined with geographically contiguous counties to form a PSU. The 1999-2000 NHANES sample is selected from a relatively small number of PSUs compared to NHANES III. With a small number of PSUs, variance estimates that account for the complex design may be relatively unstable, a factor which introduces a higher level of uncertainty in the annual estimates.
- NHANES is designed to increase precision by combining data across calendar years. Because of the relatively small sample size in 1999 and 2000, analytical data for just one or two survey participants may be weighted heavily and greatly influence the mean value reported.
- The number of geographic sites sampled each year is small and environmental exposures may vary geographically; thus producing environmental exposure estimates by geographic region using the NHANES data set is of limited value.
- The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical has caused or will cause harmful effects.

Data Sources

Centers for Disease Control and Prevention (CDC). 2003. Second National Report on Human Exposure to Environmental Chemicals. (Accessed November 21, 2004).
<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

References

Centers for Disease Control and Prevention (CDC). 2003. Second National Report on Human Exposure to Environmental Chemicals. (Accessed November 21, 2004).
<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

Pirkle JL, Flegal KM, Bernert JT, Brody DJ, Etzel RA, Maurer KR. 1996. Exposure of the U.S. Population to Environmental Tobacco Smoke: The Third National Health and Nutrition Examination Survey, 1988 to 1991. *Journal of American Medical Association* 275:1233-1240.

Graphics

Air Chapter – Indoor Air Exposure – Cotinine Levels

Table 102_107Cotinine. Selected percentiles of serum cotinine concentrations (in ng/mL) for the United States non-smoking population, aged 3 years and older, National Health and Nutrition Examination Survey (NHANES), 1999-2000

	Sample Size	10 th	25 th	50 th	75 th	90 th
Total, Age 3 years and older	5,999	<LOD	<LOD	0.06	0.24	1.02
Sex						
Male	2,789	<LOD	<LOD	0.08	0.30	1.20
Female	3,210	<LOD	<LOD	<LOD	0.18	0.85
Race Ethnicity*						
Black, non-Hispanic	1,333	<LOD	<LOD	0.13	0.50	1.43
Mexican American	2,242	<LOD	<LOD	<LOD	0.14	0.51
White, non-Hispanic	1,949	<LOD	<LOD	0.05	0.21	0.95
Age Group						
3-11 years	1,174	<LOD	<LOD	0.11	0.50	1.88
12-19 years	1,733	<LOD	<LOD	0.11	0.54	1.65
20+ years	3,052	<LOD	<LOD	<LOD	0.17	0.63

*Other racial/ethnic groups are included in the Total only

<LOD = Less than the limit of detection of 0.05 ng/mL in serum

Source: Centers for Disease Control and Prevention. 2003. Second National Report on Human Exposure to Environmental Chemicals. (Accessed November 21, 2004)

<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

R.O.E. Indicator QA/QC

Data Set Name: BLOOD COTININE LEVEL

Indicator Number: 102 (89102)

Data Set Source: CDC, NHANES

Data Collection Date: ongoing

Data Collection Frequency: two year cycles starting with 1999

Data Set Description: Blood Cotinine Level

Primary ROE Question: What are the trends in indoor air quality and it's effects on human health?

Question/Response

T1Q1 Are the physical, chemical, or biological measurements upon which this indicator is based widely accepted as scientifically and technically valid?

Yes. Blood samples were collected and processed in accordance with the methods indicated in the National Health and Nutrition Examination Survey (NHANES) Specimen Collection and Laboratory/Medical Technologists Procedures Manual (LPM). See:

<http://www.cdc.gov/nchs/data/nhanes/blood.pdf>; <http://www.cdc.gov/nchs/data/nhanes/LAB1-6.pdf>. Serum cotinine is measured by an isotope dilution high performance liquid chromatography/atmospheric pressure chemical ionization tandem mass spectrometric (ID HPLC-APCI MS/MS) method. Briefly, the serum sample is spiked with methyl-D, cotinine as an internal standard, and following an equilibration period, the sample is applied to a basified solid phase extraction column. Cotinine is extracted off the column with methylene chloride, the organic extract is concentrated, and the residue is injected onto a short, C18 HPLC column. The eluant from these injections is monitored by APCI-MS/MS, and the m/z 80 daughter ion from the m/z 177 quasi-molecular ion is quantitated, along with additional ions for the internal standard, external standard, and for confirmation. Cotinine concentrations are derived from the ratio of native to labeled cotinine in the sample by comparisons to a standard curve (http://www.cdc.gov/nchs/data/nhanes/frequency/lab06_doc.pdf). The units used for this indicator were ng/L (<http://www.cdc.gov/nchs/data/nhanes/frequency/varlab.pdf>).

T1Q2 Is the sampling design and/or monitoring plan used to collect the data over time and space based on sound scientific principles?

Yes. NHANES is designed to provide statistically representative national averages. Starting with NHANES 1999, the survey is conducted annually. All participants aged 3 years or older in NHANES 1999-2000 were measured for blood cotinine. The measurements produced by NHANES for this indicator were used in the "Second National Report on Human Exposure to Environmental Chemicals" published by the National Center for Environmental Health in 2003 (<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>).

T1Q3 Is the conceptual model used to transform these measurements into an indicator widely accepted as a scientifically sound representation of the phenomenon it indicates?

The data presented are direct measurements.

T2Q1 To what extent is the indicator sampling design and monitoring plan appropriate for answering the relevant question in the ROE?

This indicator is based on a national probability-based sampling design and is deemed of sufficient quality for generalization to the nation. The samples for 1999-2000 were used for this analysis. Quality assurance measures were in place. Beginning in 1999, NHANES became a continuous and annual survey. The sampling plan for each year follows a complex, stratified, multistage, probability-cluster design to select a representative sample of the civilian, noninstitutionalized population. Every year, approximately 7,000 individuals, of all ages, are interviewed in their homes; of these, approximately 5,000 complete the health examination component of the survey. The survey sample size for NHANES 1999-2000 is 9,965 (<http://www.cdc.gov/nchs/data/nhanes/gendoc.pdf>).

T2Q2 To what extent does the sampling design represent sensitive populations or ecosystems?

The current sampling design includes oversampling of African Americans, Mexican Americans, adolescents (12-19 year olds), older Americans (60 years of age and older), and pregnant women to produce more reliable estimates for these groups.

T2Q3 Are there established reference points, thresholds or ranges of values for this indicator that unambiguously reflect the state of the environment?

This indicator simply indicates that exposure to environmental tobacco smoke (ETS) has occurred. Cotinine is a major metabolite of nicotine and is currently regarded as the best biomarker in active smokers and in nonsmokers exposed to ETS. Nonsmokers exposed to typical levels of ETS have cotinine levels of less than 1 ng/mL, with heavy exposure to ETS producing levels in the 1-10 ng/mL range. Active smokers almost always have levels higher than 10 ng/mL, and sometimes higher than 500 ng/mL. As reported in "Second National Report on Human Exposure to Environmental Chemicals" published by the National Center for Environmental Health in 2003 (<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>). The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical has caused or will cause harmful effects.

T3Q1 What documentation clearly and completely describes the underlying sampling and analytical procedures used?

Documentation for NHANES 1999-2000 is found on NCHS/CDC website at the following URL: http://www.cdc.gov/nchs/about/major/nhanes/nhanes99_00.htm#Laboratory%20Files. The following provides more specific examples: The Addendum to the NHANES III for the 1999-2000 dataset clearly outlines the 1999-2000 sampling design and recommends analytic procedures (<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>; <http://www.cdc.gov/nchs/data/nhanes/nhanes3/nh3gui.pdf>). The "Second National Report on Human Exposure to Environmental Chemicals" published by the National Center for Environmental Health in 2003 more generally describes the NHANES 1999-2000 sampling plan (<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>). Laboratory measurement information: http://www.cdc.gov/nchs/data/nhanes/frequency/lab06_doc.pdf. And the "Weighting Notes" posted on the NHANES website also offer helpful advice (<http://www.cdc.gov/nchs/data/nhanes/frequency/weights%20to%20usev6.pdf>). Information contained in Table A1 can be found at: Centers for Disease Control and Prevention. 2003. Second National Report on Human Exposure to Environmental Chemicals. (Accessed November 21, 2004) <http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>.

T3Q2 Is the complete data set accessible, including metadata, data-dictionaries and embedded definitions or are there confidentiality issues that may limit accessibility to the complete data set?

For the most part, Individual level data are available, but data access limitations do exist for some variables due to confidentiality issues
(http://www.cdc.gov/nchs/about/major/nhanes/nhanes99_00.htm#Laboratory%20Files).

T3Q3 Are the descriptions of the study or survey design clear, complete and sufficient to enable the study or survey to be reproduced?

Yes. The Addendum to the NHANES III for the 1999-2000 dataset clearly outlines the 1999-2000 sampling design and recommends analytic procedures
(<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>;
<http://www.cdc.gov/nchs/data/nhanes/nhanes3/nh3gui.pdf>).

T3Q4 To what extent are the procedures for quality assurance and quality control of the data documented and accessible?

The quality assurance plans for NHANES 1999-2000 are available from the Division of Data Dissemination, NCHS, 6525 Belcrest Rd. Hyattsville, MD, 20782-2003. Tel. 301-458-4636.
<http://www.cdc.gov/nchs/about/quality.htm>.

T4Q1 Have appropriate statistical methods been used to generalize or portray data beyond the time or spatial locations where measurements were made (e.g., statistical survey inference, no generalization is possible)?

Yes. The NHANES 1999-2004 survey is designed to be annually nationally representative of the U.S. citizen, non-institutionalized population (see page 11 of the addendum linked below)
(<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>).

T4Q2 Are uncertainty measurements or estimates available for the indicator and/or the underlying data set?

Yes (see pages 11-19 of the addendum linked below)
(<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>).

T4Q3 Do the uncertainty and variability impact the conclusions that can be inferred from the data and the utility of the indicator?

NHANES selects a representative sample of the civilian, non-institutionalized population in the United States using a complex, stratified, multistage, probability-cluster design. Beginning in 1999, NHANES became a continuous and annual national survey. With only 2 years of data in NHANES 1999-2000, instead of the 6-years for NHANES III (1988-1994), some differences exist that may limit the underlying data with respect to completeness or representative of coverage. The sample size is smaller and the number of geographic units in the sample is more limited. The current 1999-2000 NHANES survey is nationally representative but it is subject to the limits of increased sampling error due to (1) the smaller number of individuals sampled in the annual sample and (2) the smaller number of Primary Sampling Units (PSUs) [see description below] available for each annual sample. Therefore, the sample size for any 1-year period is relatively small, possibly resulting in large variability for U.S. population estimates, especially those for narrowly defined demographic groups or other specific subgroup analyses. For NHANES 1999-2000, the first stage of selection was the PSU-level. The PSUs were defined as single counties. For a few PSUs, the county population was too small and those counties were

combined with geographically contiguous counties to form a PSU. The 1999-2000 NHANES sample is selected from a relatively small number of PSUs compared to NHANES III. With a small number of PSUs, variance estimates that account for the complex design may be relatively unstable, a factor which introduces a higher level of uncertainty in the annual estimates. NHANES is designed to increase precision by combining data across calendar years. Because of the relatively small sample size in 1999 and 2000, analytical data for just one or two survey participants may be weighted heavily and greatly influence the mean value reported. The number of geographic sites sampled each year is small and environmental exposures may vary geographically; thus producing environmental exposure estimates by geographic region using the NHANES data set is of limited value. For more information, see the addendum to NHANES III linked below: <http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>.

T4Q4 Are there limitations, or gaps in the data that may mislead a user about fundamental trends in the indicator over space or time period for which data are available?

As subsequent years are added to this survey, estimates will become more stable. However, with the laboratory data, there is no guarantee that an environmental chemical will be measured from year to year. Cotinine was measured in the next two year cycle 2001-2002 (http://www.cdc.gov/exposurereport/pdf/third_report_chemicals.pdf). Serum cotinine was measured in all people in the survey year aged three years and older. The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical has caused or will cause harmful effects.